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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,794	10/15/2003	Kent Jardemark	58073 (47137)	9727
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EXAMINER				
KOSSON, ROSANNE				
ART UNIT		PAPER NUMBER		
1652				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/688,794

Applicant(s)

JARDEMARK ET AL.

Examiner

Rosanne Kosson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-65, 67, 71, 77-79, 81-83, 85, 87-91 and 103-105 is/are pending in the application.
- 4a) Of the above claim(s) 63, 77 and 78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55-62, 64, 65, 67, 71, 79, 81-83, 85, 87-91 and 103-105 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-848)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The amendment filed on December 11, 2008 has been received and entered. Claims 55, 58-61, 67, 71, 79, 81, 83 and 90 have been amended. Claims 1-54, 66, 68-70, 72-76, 80, 84, 86 and 92-102 have been canceled. Claims 103-105 have been added. Claims 63, 77 and 78 were withdrawn in the previous Office action as being drawn to non-elected inventions. Claim 81 is labeled "original," but should be labeled "currently amended." Claim 62, elected in Applicants' response of July 7, 2008 to a restriction requirement, should be labeled "original," not "withdrawn," whereas claim 63, the non-elected species, should be labeled "withdrawn," not "original." Accordingly, claims 55-62, 64-65, 67, 71, 79, 81-83, 85, 87-91 and 103-105 to the extent that they read on the elected invention are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, second paragraph

Claims 55-62, 64-65, 67, 71, 79, 81-83, 85, 87-91 are again rejected, and claims 103-105 are rejected, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although claims 55 and 60 have been amended, they are still confusing and ambiguous in their recitation of the claimed microfluidics system, and the structure of the claimed apparatus still cannot be understood, rendering the meaning of claims unclear. As previously discussed, it is not clear if the claimed device is a one-piece structure or a two-piece structure, and Applicants

have not addressed this point. If the device is a two-piece structure, is the substrate the base (i.e., a modified microtiter plate) or is it the lid for the base?

In claim 55, the substrate comprises a measurement chamber and a raised aperture. The raised aperture comprises a tip, and the tip comprises a housing. The measurement chamber comprises a microchannel. But, the relationship of these parts is unclear, particularly the relationship of the aperture, the substrate and the measurement chamber. As previously discussed, it is not clear if the substrate is a one-piece device (a molded plate having apertures or tips, an internal or external plumbing system and wells or reservoirs) or a two-piece device (with the apertures and tips in the upper part and the plumbing and wells in the lower part). Also, it is not clear what the measurement chamber is. Additionally, the microchannel need not be connected to anything but the measuring chamber, and the measuring chamber need not be connected to anything. Thus, the structure and how the claimed apparatus is used are unclear. Claim 60 recites the same apparatus as claim 55 with the change that the aperture is a plurality of solid electrode tips. Applicants have added the functional limitation that the aperture or set of solid electrode tips can detect an electrical property of a lipid material found in cells or of a cell, but this limitation does not serve to add or clarify any structures. In their response, Applicants refer to certain drawings and indicate that these structures are encompassed by the claims. But, the claims are much broader than the embodiments shown in the drawings. Clear and definite structures must still be recited in the claims. Perhaps specific reference to the figures as a claim requirement would clarify the relationship of the components. This is commonly done in device claims. Typically when this is done, the figures provide numbered parts for reference. Since the instant figures lack reference characters as does the specification, new drawings and

amendments to the specification might be needed. It is noted that the rejection under 103 below is based in part on a broad interpretation of the device. Clarification and appropriate correction are again required.

Claim 90 is still confusing, because the phrase "scanning a cell across the aqueous streams from the microchannels" has been made more unclear by the addition of the phrase "wherein the scanning mechanism comprises translating the cells across the microchannels." As previously discussed, it cannot be determined where the cell is in the claimed microfluidics system, relative to the microchannels or the measurement chamber or the substrate. Now, Applicants have added a step to a device claim, the step of using the scanning mechanism to translate cells across the microchannels. "Translation" or "translating" is not defined in the specification. It cannot be determined what translating cells means. It cannot be determined what Applicants mean to say about the scanning mechanism and the microchannels in this claim. It cannot be determined how scanning cells translates them. Clarification and appropriate correction are again required.

Claim Rejections - 35 USC § 102

In view of Applicants' amendments to the claims, the rejection of claims 55, 57-59, 67 and 71 under 35 U.S.C. 102(b) as being anticipated by Doellgast (US 5,078,164) is withdrawn.

In view of Applicants' amendments to the claims, the rejection of claims 60, 61, 62, 64, 65, 67, 79-83, 87, 88 and 91 under 35 U.S.C. 102(b) as being anticipated by Peeters (US 6,123,819) is withdrawn.

Claim Rejections - 35 USC § 103

In view of Applicants' amendments to the claims, the rejection in the previous Office action is withdrawn and is replaced with the following rejection.

Claims 55-62, 64-65, 67, 71, 79, 81-83, 85, 87-91 and 103-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maher et al. (US 2002/0025568 A1) and He et al. (US 2003/0049862 A1) in view of Peeters (US 6,123,819) and Hamill et al. ("Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches," Pflügers Archiv 391:85-100, 1981).

Maher et al. disclose an apparatus for carrying out electrical measurements on cells. The apparatus comprises a substrate comprising an array of measurement chambers (a microtiter plate) that contain cells. The apparatus comprises an array of microelectrodes that match the wells in the microtiter plate and that are arranged in a lid or cover. The electrodes may be solid (i.e., have solid tips) or fluid filled (patch clamp electrodes). Patch clamp electrodes have a tip that is a housing that defines a lumen and that can be inserted into a cell membrane, which is a lipid-based cell structure. The tip has a contacting surface that has a diameter of about one micron, which is a value of less than about one micron, as "about one micron" includes values greater than and less than one micron. The electrode is filled with a conducting electrolyte solution (a buffered salt solution). See Figs. 1, 3 and 9 and paragraphs 11, 15, 127, 136, 137, 143, 144 and 160. See also Hamill et al., p. 86, second full paragraph and right col.; p. 91, left col.; p. 92, left col.; and Figs. 1, 2A, 6A, 9 and 10 on pp. 86, 87, 91, 93 and 94. The apparatus is part of a computer-controlled system that operates the electrical, mechanical and optical aspects of the apparatus, as it controls the activity of the electrodes, movement of the microtiter plate,

spectroscopic readings of the wells in the microtiter plate, and data collection and analysis. The electrodes are compatible with microfluidics equipment (see paragraphs 197, 198, 202 and 205-208). Maher et al. do not disclose that the measurement chambers have microchannels.

He et al. disclose a microfluidics system, in which the microfluidics plumbing is incorporated into the lid for a standard microtiter plate, thereby providing the measurement chambers with microchannels. See paragraphs 6-12 and 37-45. The measurement chambers are circular and the microchannels may be radially disposed with outlets in the chambers (see paragraph 39). The system comprises a pressure control device for controlling the positive and negative pressures to the microchannels, which fills and empties the measurement chambers, allowing assays to be performed and the chambers to be washed (see paragraph 49).

The claimed microfluidics system is the apparatus of Maher et al. in which the microtiter plate lid has been modified with the microfluidics plumbing of He et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the microtiter plate of Maher et al. with the microfluidics plumbing for microtiter plate lids of He et al., because He et al. disclose that this modification transforms the apparatus into high-throughput apparatus, using standard industry equipment, for carrying out the most common types of automated assays used in the biotechnology and pharmaceutical industries, biochemical and genomics assays. Microfluidics chips, by comparison, require specialized custom equipment and have much lower throughput, i.e., they perform far fewer assays in the same amount of time (see paragraphs 6-7).

Regarding claim 71, in modifying the apparatus of Maher et al. with the microfluidics plumbing of He et al., the plumbing (microchannel tubing) would have been inserted in the lid,

which is a substrate that is attached to the measurement chambers (see Maher et al., Figs. 1A, 1B and 3). Thus, the substrate comprises measurement chambers. The portion of the microtiter plate that holds the wells is also a substrate. As a result, both the microtiter plate substrate and the lid substrate would have been interfaced to the multi-well plate via the external tubing, because the tubing connects the different portions of the microtiter plate and the lid via fluid flow (see He et al., paragraphs 43-44 and Figs. 3-4). As a result, this feature does not distinguish the claimed invention over the prior art.

Regarding the computer-controlled equipment for manipulating the microfluidics system (claims 79, 81-83 and 87-91), as previously discussed, Peeters discloses a microfluidics system comprising a nanoelectrode array on a substrate in a measuring chamber that holds fluids. The array and the chamber are connected to a microfluidics system for the delivery and removal of materials to and from the array via microchannels. The array is connected to a microcontroller or microprocessor, which analyzes signals from the microelectrodes and controls the microfluidics system. The pressure in the microchannels is controlled by an external micro-pump (see Figs. 1-3 and 5; col. 3, lines 21-35; and col. 8, line 38, to col. 9, line 7). Scanning of the nanoelectrode array in the x-y plane at specific positions is computer-controlled and very precise, similar to scanning a DNA chip, and scanning may be performed with a laser. Thus, the laser can scan a cell structure such as protein on the array relative to a microchannel outlet when the chip array of Figs. 1-3 is used in one of the chambers in Fig. 5. Signals from the electrodes can be amplified via transistors. See col. 10, lines 20-30; and col. 10, line 41, to col. 11, line 6). It would have been obvious to one of ordinary skill in the art at the time of the invention to use the computer-controlled equipment of Peeters with apparatus of Maher et al. (modified with the

plumbing of He et al.), because, as noted above, Maher et al. disclose that their apparatus is designed for use with computer-controlled equipment. Peeters discloses the same computer-controlled equipment but is more explicit about the specific tasks and operations that the equipment performs.

Regarding claim 85, as previously discussed, Peeters does not disclose that the operation of the scanning mechanism (e.g., the rate, direction or number of repetitions of scanning) is responsive to a signal from the detector. But, it would have been obvious to one of ordinary skill in the art at the time of the invention that, if an electrode or a portion of an electrode array, during an experiment, showed one or more regions of interest (e.g., particularly high or low amounts of bound molecules or cell fragments), the software controlling the scanner would have been manipulated to scan in greater detail those regions of interest. Those regions of interest would have been scanned at a different speed to obtain better resolution, and multiple scans would have been performed. Therefore, this claim does not distinguish the claimed invention over the prior art.

Regarding claim 90, as discussed above, it cannot be determined from the claim language where the cell that is scanned is located in one of the microchannels or in the apparatus or what translating is. Nevertheless, in order to proceed with examination, the claim appears to mean that the imaging information for a cell is retained as the microchannels are scanned. A scanner can scan the cells, but it cannot move them. The laser scanner and the imaging equipment would have been readily programmed by one of ordinary skill in the art at the time of the invention to detect one or more cells at any desired location within a measurement chamber or within a microchannel and to scan the entirety of the measurement chambers and the microchannels (i.e.,

the entire microtiter plate). Therefore, this claim does not distinguish the claimed invention over the prior art.

In view of the foregoing, a holding of obviousness is required.

Conclusion

No claim is allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is (571)272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652
rk/2008-12-31

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657